

II.B.4.

Indeed, the scientific consensus holds that nonpharmacological factors are important to consumers only because they are linked to the pharmacological effects of nicotine. Thus, Jed Rose, one of the key researchers cited by the industry to support the contention that consumers use tobacco for nonpharmacological reasons, refers to nonpharmacological factors as “sensory cues” that are used to meter nicotine intake.³⁸⁸

As described in section II.B.3., above, such cues become “conditioned” as they are associated with the pharmacological effects of nicotine on the brain. These environmental factors are certainly important to tobacco consumers, as they are to users of other addictive drugs,³⁸⁹ but they are not the primary reasons for use. As a tobacco industry executive in a speech to the company’s board of directors said:

[T]he psychosocial motive is not enough to explain continued smoking. Some other motive force takes over to make smoking rewarding in its own right. Long after adolescent preoccupation with self-image has subsided, the cigarette will even preempt food in times of scarcity on the smoker’s priority list . . . We are of the conviction . . . that the ultimate explanation for the perpetuated cigarette habit resides in the pharmacological effect of smoke upon the body of the smoker, the effect being most rewarding to the individual under stress.³⁹⁰

2. The cigarette manufacturers cite research suggesting that nicotine-free cigarettes have flavor³⁹¹ and may help smokers to quit.³⁹² They draw particular attention

³⁸⁸ Rose JE, Behm FM, Levin ED, Role of nicotine dose and sensory cues in the regulation of smoke intake, *Pharmacology, Biochemistry and Behavior* 1993;44:891-900. See AR (Vol. 8 Ref. 100).

³⁸⁹ Surgeon General’s Report, 1988, at 59. See AR (Vol. 129 Ref. 1592).

³⁹⁰ Wakeham H (Philip Morris, Inc.), *Smoker Psychology Research*, presented to Philip Morris board of directors (Nov. 26, 1969), at 237, 240. See AR (Vol. 11 Ref. 142).

³⁹¹ Levin ED, Behm FM, Rose JE, The use of flavor in cigarette substitutes, *Drug and Alcohol Dependence* 1990;26:155-160, at 159. See AR (Vol. 535 Ref. 96, IIIJ).

³⁹² Butschky MF, Bailey D, Henningfield JE, Pickworth WB, Smoking without nicotine delivery decreases withdrawal in 12-hour abstinent smokers, *Pharmacology, Biochemistry and Behavior* 1995;50(1):91-96. See AR (Vol. 442 Ref. 7484).

II.B.4.

to a recent presentation by Rose *et al.*, in which smokers given a denicotinized cigarette reported the same or slightly less relief of craving than smokers given intravenous nicotine, and less relief than smokers given their usual brand of cigarettes.³⁹³ They also reported more immediate satisfaction from the denicotinized cigarette than from intravenous nicotine, although less than from their usual brand. The denicotinized cigarette provided less psychological reward than did intravenous nicotine. The smokeless tobacco manufacturers also suggest that no-nicotine substitutes for smokeless tobacco may have helped some users remain abstinent. According to the industry, this research demonstrates that consumers use tobacco products for reasons other than nicotine.

FDA disagrees. The cited studies do suggest that low- or no-nicotine products can be used in research and in a small proportion of former users of tobacco products. Yet the products have been uniformly rejected by *tobacco consumers*, who do not view them as acceptable substitutes for cigarettes. When given a choice, tobacco users will not abandon nicotine for flavor, demonstrating the real reason they smoke. For example, Next, a denicotinized cigarette that was briefly marketed by Philip Morris, was removed from the market because, according to the company, it was not accepted by consumers.

The cited studies replicate many others that show that the most consistent and strongest effects are produced by nicotine-delivering cigarettes. It is not surprising that nicotine injections, which, according to the studies produced significant pain and burning at the site of injection, do not produce all the satisfaction of smoking nor duplicate the

³⁹³ Rose JE, Westman EC, Behm FM, Comparative effects of intravenous nicotine and de-nicotinized cigarette smoke, poster presented at the annual meeting of the Society for Research on Nicotine and Tobacco (Mar. 15-17, 1996), Washington, D.C. See AR (Vol. 711 Ref. 21).

II.B.4.

taste and throat sensations of smoking. As described in section II.B.3., above, the efficacy of nicotine-free cigarettes in alleviating some of the symptoms of withdrawal is consistent with the conclusion that social and environmental factors become associated with obtaining the pharmacological effects of nicotine, and thus are perceived as pleasurable as a “conditioned response,” but in and of themselves are not the reason people smoke. Low- or no-nicotine cigarettes may temporarily provide some relief to consumers as a result of the conditioned response to the sensorimotor aspects of smoking, but this response is subject to “rapid extinction” when nicotine is withheld.³⁹⁴ This phenomenon is similar to the temporary finding that heroin addicts feel pleasure from injecting themselves with saline.³⁹⁵

The study by Rose is entirely consistent with these findings. The study evaluated only the immediate effects of a denicotinized cigarette on craving reduction, satisfaction, and psychological reward. It did not attempt to evaluate any effects of denicotinized cigarettes on sustained satisfaction or relief of withdrawal symptoms. Rose himself has stated that smokers seek the sensory cues of smoking because “the repetition of the smoking act thousands of times per year by a moderately heavy smoker leads to a strong conditioned association between the sensory aspects of smoking . . . and the pharmacological effects of nicotine.”³⁹⁶ Therefore, according to Rose, “effective

³⁹⁴ *Id.*

³⁹⁵ O'Brien CP, Testa T, Ternes J, Greenstein R, Conditioning effects of narcotics in humans, in *Behavioral Tolerance: Research and Treatment Implications*, NIDA Research Monograph 18 (Washington DC: Government Printing Office No. 017-024-00899-8, Jan. 1978), at 67-71. See AR (Vol. 535 Ref. 96, vol. III.L).

³⁹⁶ Rose JE, Levin ED, Inter-relationships between conditioned and primary reinforcement in the maintenance of cigarette smoking, *British Journal of Addiction* 1991;86:605-609, at 605. See AR (Vol. 67 Ref. 58).

II.B.4.

treatment of tobacco abuse needs to take into account the influence of these sensory cues,”³⁹⁷ by, for example, providing the smoker with de-nicotinized cigarettes, in addition to strategies to eliminate nicotine dependency.³⁹⁸ He is explicit, however, that nicotine is the primary reinforcer of smoking behavior, and that desire for the sensory aspects of tobacco use is the result of conditioned reinforcement maintained by nicotine’s primary reinforcement.³⁹⁹

3. To support the argument that consumers use tobacco products for flavor, the tobacco industry cites research in which smokers’ satisfaction with smoking decreased when their upper airways were anesthetized.

Upon review of this research, FDA finds that the studies do not support the contention that consumers smoke cigarettes primarily for flavor. As described above, the researcher who led the study, Rose, believes that nonpharmacological factors associated with tobacco consumption are “cues” important to smokers only by association with nicotine’s pharmacological impact.

Moreover, the research cited does not establish that the reason for the drop in smoking satisfaction upon airway anesthetization was the blockade of sensory input from smoke. These decreases in satisfaction might have been due simply to the unpleasant sensation of upper airway anesthetization, not to any blockade of sensory input from smoke. In this study, satisfaction with “sham smoke” also dropped with anesthesia. Sham smoke was so diluted as to provide few pharmacological or sensory effects. Thus,

³⁹⁷ *Id.*

³⁹⁸ *Id.* at 607.

³⁹⁹ *Id.* at 605-606.

II.B.4.

providing anesthesia decreased the satisfaction of consuming real cigarette smoke *and placebo smoke*.⁴⁰⁰

The study does, however, provide data addressing the importance of the pharmacological aspects of smoking. Thirty minutes after smoking, the subjects who had received smoke delivering nicotine—*regardless of whether their throats had been anesthetized*—felt similarly satisfied. And their satisfaction was greater than that of those who had received “sham smoke.” Thus, the study indicated that nicotine produces smoking satisfaction *even in the absence of mouth and throat sensation*.

4. The tobacco industry cites three studies to support the argument that consumers use tobacco products out of “habit and ritual.”

Upon review of these studies, FDA concludes that they provide no evidence that “habit and ritual” are the primary motivation for use of tobacco products. As described at length above, “habit and ritual” are important to consumers of all addictive drugs, but only through their linkage to the pharmacological effects of the drug.

First, the industry cites a study in which some smokers did not consider the first cigarette of the day their favorite.⁴⁰¹ The observation relates to a detail of smoking rather than to underlying motivation; as described in section II.B.3., above, there are many reasons why an individual may desire a particular cigarette at a particular time. This is not evidence that “habit or ritual” is the driving biological force for maintenance of tobacco use.

⁴⁰⁰ Rose JE, Tashkin DP, Ertle A, Zinser MC, Lafer R, Sensory blockade of smoking satisfaction, *Pharmacology, Biochemistry and Behavior* 1985;23:289-293, at 290 (emphasis added). See AR (Vol. 42 Ref. 124).

⁴⁰¹ Jarvik M, Killen JD, Varady A, Fortmann SP, The favorite cigarette of the day, *Journal of Behavioral Medicine* 1993;16:413-422. See AR (Vol. 535 Ref. 96, III.A).

II.B.4.

The industry then quotes the speculative conclusion of a study without any description of the research. In fact, the study's main finding was that the smell of cigarettes was *not* important for smoking behavior.⁴⁰²

The industry cites another conclusion of a study without any description of the research.⁴⁰³ One of the study's major findings was that enforced abstinence (smokers were not allowed to smoke for an afternoon) had different effects on subsequent smoking behavior than natural abstinence (smokers did not smoke while asleep at night). Basic biological imperatives undoubtedly affect the details of smoking behavior but certainly cannot explain the reason for tobacco use.

5. The tobacco industry argues that the "social aspects" of smoking explain consumer use of tobacco. No studies are cited to support this conclusion. As the Surgeon General's Report noted in 1988, social factors influence initiation and patterns of use of many addictive drugs;⁴⁰⁴ the primary reason for the drug's use, however, is pharmacological. In this respect, nicotine is similar to heroin.⁴⁰⁵

6. The smokeless tobacco industry argues that the evidence cited by FDA in support of its conclusion that consumers use tobacco products nearly exclusively for pharmacological effects has little to do with smokeless tobacco. Five studies were

⁴⁰² Baldinger B, Hasenfratz M, Battig K, Switching to ultralow nicotine cigarettes: effects of different tar yields and blocking of olfactory cues, *Pharmacology, Biochemistry and Behavior* 1995;50(2):233-239, at 238. See AR (Vol. 535 Ref. 96, vol. III.A).

⁴⁰³ Jacober A, Hasenfratz M, Battig K, Cigarette smoking: habit of nicotine maintenance? *Human Psychopharmacology* 1994;9:117-123, at 117. See AR (Vol. 535 Ref. 96, vol. III.G).

⁴⁰⁴ Surgeon General's Report, 1988, at 15. See AR (Vol. 129 Ref. 1592).

⁴⁰⁵ Jaffe JH, Drug addiction and drug abuse, in *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 8th ed. (New York: Pergamon Press, 1990), chap. 22 (522-573), at 529. See AR (Vol. 535 Ref. 96, vol. III.G).

II.B.4.

submitted with the comment that are claimed to demonstrate that smokeless tobacco consumers use those products because they “enjoy the taste” or simply “like it,” not for any “pharmacological effects.”⁴⁰⁶

FDA disagrees with the industry’s interpretation of these studies. As discussed in section II.B.3., above, when people use drugs with powerful pharmacological effects such as nicotine they commonly associate many environmental stimuli with the pleasurable experience of consuming the substance. Thus, a survey result that consumers “enjoy the taste” indicates only that a significant portion of consumers have linked the sensory cues to the pharmacological effects of nicotine.

None of the five studies cited by the industry noted whether users who did not give pharmacological reasons for using smokeless tobacco had ever tried to quit. Thus, many of these users may not have been aware of their pharmacological addiction. As an expert quoted by the Inspector General of the Department of Health and Human Services

⁴⁰⁶ Walsh MM, Hilton JF, Ernster VL, Masouredis CM, Grady DG, Prevalence, patterns, and correlates of spit tobacco use in a college athlete population, *Addictive Behavior* 1994;19:411-427. See AR (Vol. 526 Ref. 95, vol. VIII).

Lopez LC, Smokeless tobacco consumption by Mexican-American university students, *Psychology Reports* 1994;75:279-284. See AR (Vol. 526 Ref. 95, vol. VIII).

Glover ED, Laflin M, Flannery D, Albritton DL, Smokeless tobacco use among American college students, *Journal of American College Health* 1989;38:81-84. See AR (Vol. 526 Ref. 95, vol. VII).

Wisniewski JF, Bartolucci AA, Comparative patterns of smokeless tobacco usage among major league baseball personnel, *Journal of Oral Pathology and Medicine* 1989;18:322. See AR (Vol. 526 Ref. 95, vol. VIII).

Connolly GN, Orleans GT, Kogan M, Use of smokeless tobacco in major-league baseball, *New England Journal of Medicine* 1988;318(19):1281-1285. See AR (Vol. 526 Ref. 95, vol. VII).

II.B.4.

explained, "Many haven't tried to quit. But when we tell them the health consequences, and then they try to quit, they can't."⁴⁰⁷

In studies cited by the industry, some users of smokeless tobacco stated that they "enjoy the taste," but a significant percentage of these users also reported that they use smokeless tobacco for psychological reasons. For example, in one study, a majority of 195 users of snuff and chewing tobacco reported using tobacco for one or more pharmacological effects, including relieving stress, relief of "strong cravings," and relieving the discomfort of withdrawal.⁴⁰⁸ These statements support the conclusion that the majority of people who use smokeless tobacco do so for the well-established pharmacological effects of nicotine: stimulation, sedation, and addiction. These studies thus constitute additional evidence that smokeless tobacco is primarily used by consumers to obtain the pharmacological effects of nicotine.

⁴⁰⁷ Department of Health and Human Services, Office on Smoking and Health, *Spit Tobacco and Youth* (Washington DC: Government Printing Office, 1992), at 8. See AR (Vol. 7 Ref. 76).

⁴⁰⁸ Walsh MM, Hilton JF, Ernster VL, Masouredis CM, Grady DG, Prevalence, patterns, and correlates of spit tobacco use in a college athlete population, *Addictive Behavior* 1994;19:411-427. See AR (Vol. 526 Ref. 95, vol. VIII).

II.C.

C. THE STATEMENTS, RESEARCH, AND ACTIONS OF THE CIGARETTE MANUFACTURERS SHOW THAT THE MANUFACTURERS INTEND THEIR PRODUCTS TO AFFECT THE STRUCTURE AND FUNCTION OF THE BODY

In sections II.A. and II.B., above, the Agency has concluded that cigarettes and smokeless tobacco are intended to affect the structure and function of the body on the basis of the foreseeable pharmacological effects and uses of cigarettes and smokeless tobacco and the widespread actual use of cigarettes and smokeless tobacco by consumers for pharmacological purposes. In this section, the Agency considers another category of persuasive evidence of intended use: the statements, research, and actions of the cigarette manufacturers themselves. In section II.D., below, the Agency considers the statements, research, and actions of the smokeless tobacco manufacturers.

The administrative record includes extensive evidence of the cigarette manufacturers' statements, research, and manufacturing practices. Much of this evidence has only recently become available as a result of the Agency's investigation, congressional hearings, and other investigations and sources. This evidence is part of the relevant objective evidence that the Agency may consider in determining the manufacturer's "intended uses" of a product.

In the Jurisdictional Analysis, the Agency made extensive findings based on the evidence then available regarding the statements, research, and actions of the cigarette manufacturers. FDA received comments on these findings from the individual tobacco companies and tobacco industry trade associations, as well as from public health organizations and other interested groups and members of the public. After careful consideration of the evidence in the record and the public comments, the Agency finds that

II.C.

the evidence described in this section provides a third independent basis for concluding that cigarettes are in fact intended to affect the structure and function of the bodies of smokers.

In section II.C.1., FDA discusses its legal authority to consider evidence of the manufacturers' statements, research, and actions in establishing intended use. This discussion shows that an intent to affect the structure or function of the body can be established by evidence showing that (1) the manufacturer "has in mind" that the product will be used by consumers for pharmacological purposes, or (2) the manufacturer has "designed" the product to provide pharmacological effects. The Agency's role in making these determinations is that of a fact finder. It weighs the statements, research, and actions of the manufacturer to determine the particular uses the manufacturer has in mind or designs its product to provide.

The Agency's fact-finding task has been made more difficult by the manufacturers' general refusal to cooperate with the Agency's investigation. Although some manufacturers did permit FDA investigators to visit their manufacturing plants in the spring of 1994, the manufacturers have failed to provide FDA with information and documents requested by FDA in July 1994 regarding nicotine in cigarettes.⁴⁰⁹ In particular, the manufacturers have failed to comply with FDA's request for company documents regarding the pharmacological effects of nicotine and the role of nicotine in cigarette design and manufacturing. The limited number of company documents provided

⁴⁰⁹ See, e.g., Letter from Chesemore RG (FDA) to Bible GC (Philip Morris Inc.) (Jul. 11, 1994). See AR (Vol. 54 Ref. 617). Similar letters were sent to other cigarette and smokeless tobacco manufacturers.